

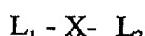
10/033,308

Attorney Docket No. 13716  
2058-181**AMENDMENTS TO THE CLAIMS**

Please amend Claims 1, 12, and 20 and add new Claims 26-29 as follows:

1. (Currently Amended) A method of attaching a biological molecule to a solid support having at least one available amino group, the method comprising:

(a) reacting the available amino group on the solid support with an activating compound, the activating compound having the structure:



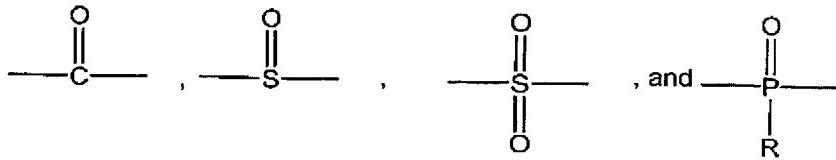
wherein  $L_1$  and  $L_2$  are leaving groups, and  $X$  is a moiety capable of nucleophilic substitution so that the reaction results in  $L_1$  being displaced by the available amino group on the solid support to form an activated support;

(b) providing a biological molecule having at least one reactive amino, thiol, or hydroxyl group, the biological molecule selected from the group consisting of oligonucleotides, nucleic acids, polypeptides, polypeptide chains, and carbohydrates; and

(c) reacting the biological molecule with the activated support, thereby displacing  $L_2$  and covalently attaching the biological molecule to the solid support.

2. (Previously Presented) A method according to claim 1 wherein one or both of  $L_1$  and  $L_2$  are each independently selected from the group consisting of halogen, imidazole, triazole, pyrrole, pyrazole, thiazole, tetrazole, and O-Aryl-R, and wherein R is selected from the group consisting of halogen, nitro, cyano, and alkoxy moiety.

3. (Previously Presented) A method according to claim 2 wherein X is selected from the group consisting of:



10/033,308

Attorney Docket No. 13716  
2058-181

wherein

R is selected from the group consisting of alkyl, aryl, and OR<sup>1</sup>;

R<sup>1</sup> is selected from the group consisting of alkyl and aryl; and wherein

the alkyl and aryl groups have having no greater than about 18 carbon atoms.

4. (Previously Presented) A method according to claim 1 wherein the activating compound is 1,2,4-carbonyl di-triazole.
5. (Previously Presented) A method according to claim 1 wherein step (b) comprises depositing between about 5 to about 25 nanoliters of the biological molecule in a circular spot at one or more sites on the activated support, wherein the circular spot has a diameter of between about 10 microns to about 500 microns at one or more sites on the activated support.
6. (Previously Presented) A method according to claim 5 wherein one or both of the activating compound and the biological molecule is printed onto the solid support.
7. (Previously Presented) A method according to claim 1 wherein in one or both of step (b), and step (c), the reaction occurs in a humid chamber.
8. (Previously Presented) A method according to claim 6 wherein in one or both of step (b), and step (c), the reaction occurs in a humid chamber.
9. (Previously Presented) A method according to claim 1 wherein step (a) occurs in an organic solution.
10. (Previously Presented) A method according to claim 9 wherein step (a) occurs in the presence of a tertiary organic base.

10/033,308

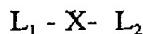
Attorney Docket No. 13716  
2058-181

11. (Previously Presented) A method according to claim 10 wherein step (c) occurs in an aqueous solution.

12. (Currently Amended) A method of attaching a biological molecule having at least one reactive amino, thiol or hydroxyl group to a solid support, the method comprising:

(a) providing a solid support having at least one available amino group, the solid support selected from the group consisting of a bead, a plate, and a film;

(b) reacting the available amino group on the solid support with an activating compound, the activating compound having the structure:

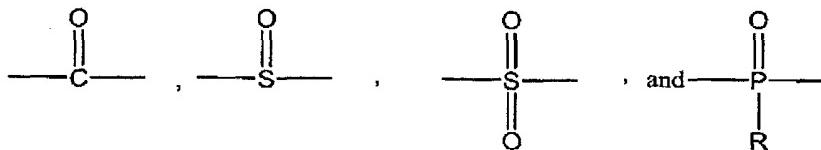


wherein  $L_1$  and  $L_2$  are leaving groups, and  $X$  is capable of nucleophilic substitution so that the reaction results in  $L_1$  being displaced by the available amino group on the solid support to form an activated support; and

(c) reacting the biological molecule with the activated support, thereby displacing  $L_2$  and covalently attaching the biological molecule to the solid support.

13. (Previously Presented) A method according to claim 12 wherein one or both of  $L_1$  and  $L_2$  are each independently selected from the group consisting of halogen, imidazole, triazole, pyrrole pyrazole, thiazole, tetrazole, and O-Aryl-R, and wherein R is selected from the group consisting of halogen, nitro, cyano, and alkoxy moiety.

14. (Previously Presented) A method according to claim 13 wherein X is selected from the group consisting of:



10/033,308

Attorney Docket No. 13716  
2058-181

wherein

R is selected from the group consisting of alkyl, aryl, and OR<sup>1</sup>;

R<sup>1</sup> is selected from the group consisting of alkyl and aryl, and wherein the alkyl and aryl groups have no greater than about 18 carbon atoms.

15. (Previously Presented) A method according to claim 12 wherein the activating compound is 1,2,4-carbonyl di-triazole.

16. (Cancelled)

17. (Cancelled)

18. (Previously Presented) A method according to claim 1 further comprising the step of washing from the solid support non-bound compounds after step (a) and before step (c).

19. (Cancelled)

20. (Currently Amended) A method of attaching a biological molecule to a solid support comprising:

(a) providing a solid support having at least one available amino group, the solid support being formed from a material selected from the group consisting of a bead, a plate, and a film cellulose, agarose, polypropylene, polystyrene, polymethacrylate, and nylon;

(b) reacting the available amino group on the solid support with an activating compound, the activating compound having the structure:

L<sub>1</sub> - X - L<sub>2</sub>

wherein L<sub>1</sub> and L<sub>2</sub> are leaving groups, and X is a moiety capable of nucleophilic substitution so that the reaction results in L<sub>1</sub> being displaced by the available amino group on the solid support to form an activated support;

10/033,308

Attorney Docket No. 13716  
2058-181

- (c) providing a biological molecule having at least one reactive amino, thiol, or hydroxyl group, the biological molecule selected from the group consisting of oligonucleotides, nucleic acids, polypeptides, polypeptide chains, and carbohydrates; and
- (d) reacting the biological molecule with the activated support, thereby displacing L<sub>2</sub> and covalently attaching the biological molecule to the solid support.

21. (Previously Presented) A method according to claim 20 further comprising the step of washing from the solid support non-bound compounds after step (b) and before step (d).

22. (Previously Presented) A method according to claim 20 wherein step (b) comprises depositing between about 5 to about 25 nanoliters of the biological molecule in a circular spot at one or more sites on the activated support, wherein the circular spot has a diameter of between about 10 microns to about 500 microns at one or more sites on the activated support.

23. (Previously Presented) A method according to claim 20 wherein one or both of the activating compound and the biological molecule is printed on the solid substrate.

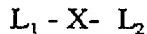
24. (Previously Presented) A method according to claim 20 wherein in one or both of step (b) and step (d), the reaction occurs in a humid chamber.

25. (Previously Presented) A method according to claim 20 wherein the biological molecule is an oligonucleotide having at least one free amino or thiol group.

26. (New) A method of attaching a biological molecule to a solid support comprising:

- (a) providing a solid support comprised of an organic polymer having at least one available amino group;
- (b) reacting the available amino group on the solid support with an activating compound, the activating compound having the structure:

10/033,308

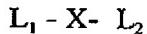
Attorney Docket No. 13716  
2058-181

wherein  $L_1$  and  $L_2$  are leaving groups, and  $X$  is a moiety capable of nucleophilic substitution so that the reaction results in  $L_1$  being displaced by the available amino group on the solid support to form an activated support;

- (c) providing a biological molecule having at least one reactive amino, thiol, or hydroxyl group; and
- (d) reacting the biological molecule with the activated support, thereby displacing  $L_2$  and covalently attaching the biological molecule to the solid support.

27. (New) A method of attaching a biological molecule to a solid support, the method comprising:

- (a) providing solid support having at least one available amino group, the solid support being formed from a material selected from the group consisting of cellulose, agarose, polypropylene, polystyrene, polymethacrylate, and nylon;
- (b) reacting the available amino group on the solid support with an activating compound, the activating compound having the structure:



wherein  $L_1$  and  $L_2$  are leaving groups, and  $X$  is capable of nucleophilic substitution so that the reaction results in  $L_1$  being displaced by the available amino group on the solid support to form an activated support;

- (c) providing a biological molecule having at least one reactive amino, thiol, or hydroxyl group; and
- (d) reacting the biological molecule with the activated support, thereby displacing  $L_2$  and covalently attaching the biological molecule to the solid support.

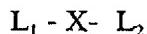
28. (New) A method of attaching a biological molecule to a solid support comprising:

- (a) providing a solid support having at least one available amino group;

10/033,308

Attorney Docket No. 13716  
2058-181

(b) reacting the available amino group on the solid support with an activating compound, the activating compound having the structure:



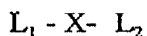
wherein  $L_1$  and  $L_2$  are leaving groups, and  $X$  is a moiety capable of nucleophilic substitution so that the reaction results in  $L_1$  being displaced by the available amino group on the solid support to form an activated support;

(c) providing a biological molecule, wherein the biological molecule is a biological macromolecule having at least one reactive amino, thiol, or hydroxyl group; and

(d) reacting the biological molecule with the activated support, thereby displacing  $L_2$  and covalently attaching the biological molecule to the solid support.

29. (New) A method of attaching a biological molecule to a solid support comprising:

(a) providing a solid support having at least one available amino group;  
(b) reacting the available amino group on the solid support with an activating compound, the activating compound having the structure:



wherein  $L_1$  and  $L_2$  are leaving groups, and  $X$  is a moiety capable of nucleophilic substitution so that the reaction results in  $L_1$  being displaced by the available amino group on the solid support to form an activated support;

(c) providing a biological molecule, wherein the biological molecule is selected from the group consisting of hormones, therapeutic drugs, and drugs of abuse; and

(d) reacting the biological molecule with the activated support, thereby displacing  $L_2$  and covalently attaching the biological molecule to the solid support.